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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,124	06/30/2005	Lai-Xi Wang	014835-178.02-011	4516

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EXAMINER
KINSEY WHITE, NICOLE ERIN

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,124	WANG, LAI-XI	
	Examiner	Art Unit	
	Nicole Kinsey White, PhD	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8-24 and 26-34* is/are pending in the application.

4a) Of the above claim(s) *15-24 and 26-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8 and 10-13* is/are rejected.

7)☒ Claim(s) *9 and 14* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/ are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/6/2005, 2/6/2006, 9/12/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of Group I (claims 1-14) in the reply filed on November 16, 2007 is acknowledged. The traversal is on the ground that the inventions are not distinct. This is not found persuasive.

35 U.S.C. § 121 (Divisional applications) states that if two or more independent and distinct inventions are claimed in one application, the Director may require the application to be restricted to one of the inventions. If the other invention is made the subject of a divisional application which complies with the requirements of section 120 of this title it shall be entitled to the benefit of the filing date of the original application.

Because this application is a filing under 35 U.S.C. § 371, the determination of "independent and distinct inventions" is made in accordance with PCT Rule 13, in particular 13.1 and 13.2 as indicated below.

13.1 - The international application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention").

13.2 - Where a group of inventions is claimed in one and the same international application, the requirement of unity of invention referred to in Rule 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

As stated in the Office Action dated October 15, 2007, the technical feature shared among the inventions listed as Groups I-V is at least two high-mannose oligosaccharide cluster on a scaffolding framework. The noted shared technical feature does not provide a contribution over the prior art, as evidenced by the teachings of Kuo et al. (WO 98/04272). Kuo et al. discloses mannose-containing oligosaccharides. Page 15 states "a suitable oligosaccharide e.g. Man_8 or Man_9, can be assembled in multivalent form by linking one or more of such molecules to a scaffold carrier molecule, thus providing a plurality of "high mannose-type" structures on a single molecule using methods known in the art." Hence, in the absence of a contribution over the prior art, the noted shared technical feature is not a shared special technical feature. Without a shared special technical feature, the inventions listed as Groups I-V lack unity with one another.

Accordingly, the requirement is still deemed proper and is therefore made FINAL.

Claim Objections

Claim 8 is objected to because of the following informalities: Claim 8 recites a colon and comma after Man_8. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 13 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claim is drawn to a pharmaceutical composition for reducing the effects of HIV, the composition comprising a therapeutically effective amount of a high-mannose oligosaccharide cluster comprising four Man9 covalently attached to a galactose scaffolding framework that is conjugated to the immunogenic protein keyhole limpet hemocyanin.

Applicants have not shown that the clustered scaffolding structure with the KLH antigen is capable of inducing an immune response against HIV that would provide the beneficial effects described on page 10, lines 8-12, of the specification. How does an immune response against KLH benefit efforts to reduce HIV? Page 21, lines 8-13, of the specification discuss the KLH construct being highly immunogenic. Other than that statement, there is no teaching or guidance in the specification that would lead one of ordinary skill in the art to expect the KLH construct to induce an immune response that can reduce HIV infectivity.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6, 8 and 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuo et al. (WO 98/04272) in view of Wittmann et al. (Peptides: The Wave of the Future, 2001, pages 174-176) and Maddon et al. (WO 00/18432).

The claims are drawn to, *inter alia*, a high-mannose oligosaccharide cluster comprising at least two high-mannose oligosaccharides positioned on a scaffolding framework, wherein the scaffolding framework comprises monosaccharides, cyclic peptides, cyclic organic compounds, or 11-bis-maleimidetetraethyleneglycol.

Kuo et al. discloses pharmaceutical compositions comprising high-mannose structures that are Man_6 – Man_{10} (see page 9, line 18 to page 11, line 26). The high-mannose structures taught by Kuo et al. may be modified to create analogs or derivatives (see page 14, line 13 to page 15, line 2). Further, Kuo et al. discloses that suitable oligosaccharides, e.g. Man_8 or Man_9, can be assembled in multivalent form by linking one or more of such molecules to a scaffold carrier molecule, thus providing a plurality of "high mannose-type" structures on a single molecule using methods known in the art. Kuo et al. further states that carbohydrates with an initial lower inhibiting activity can find beneficial use if made multivalent, i.e., linked to a common carrier with

suitable spacing. The carrier can be any known inert molecule to which the carbohydrates of interest can be bound using known chemistries. The carrier can be a synthetic molecule or an isolated naturally occurring molecule. Such bivalent or multivalent binding sites could demonstrate an enhanced avidity for a ligand and thus inhibit binding much more efficiently (see page 15, lines 3-26).

Kuo et al. does not specifically teach carriers or scaffolding comprising monosaccharides, cyclic peptides, cyclic organic compounds, or 11-bis-maleimidetetraethyleneglycol. However, Wittmann et al. teaches the use of cyclic peptides as scaffolds for multivalent presentation of carbohydrate epitopes. Wittmann et al. teaches that these cyclic peptides are useful as scaffolds because they allow the generation of spatial diversity in two dimensions. Positional diversity generates different carbohydrate patterns displayed on the scaffolds, and varying the stereochemistry of the amino acids increases spatial diversity by generating different backbone folds (see pages 174-175).

Therefore, it would have been obvious to one of ordinary skill in the art to attach the high-mannose structures taught by Kuo et al. to a carrier such as a cyclic peptide. One would have been motivated to do so given the suggestion by Kuo et al. to link high-mannose structures to a common carrier, which can be can be a synthetic molecule or an isolated naturally occurring molecule, to create multivalent molecules with enhanced avidity for a ligand and thus inhibit binding much more efficiently. There would have been a reasonable expectation of success given the knowledge that others, such as

Whittmann et al., have used cyclic peptides as scaffolding for the multivalent presentation of carbohydrate epitopes.

With regard to claim 2, it would have been obvious to also attach four or more high-mannose structures to a common carrier to create multivalent structures with enhanced avidity for a ligand and thus inhibit binding much more efficiently as taught by Wittmann et al.

Kuo et al. also does not teach conjugating the high-mannose structures to an immunogenic protein. However, Maddon et al. (Carbohydrate Vaccines for Viral diseases) teaches that the immunogenicity of purified carbohydrates can be improved via their conjugation to immunogenic carrier proteins (e.g., diphtheria toxiod, tetanus toxoid, the outer membrane protein complex of Neisseria meningitides, and keyhole limpet hemocyanin), which resulted in an isotype switch from a IgM response of short duration to a long lasting, high affinity IgG response indicating that activation of T-cell dependent pathways against carbohydrates is likely to occur (see pages 2-4).

Accordingly, it would have been obvious to one of ordinary skill in the art to conjugate the high-mannose structures taught by Kuo et al. to a carrier protein. One would have been motivated to do so given the suggestion by Maddon et al. that conjugating carbohydrates to immunogenic carrier proteins improves the immunogenicity of the carbohydrate. There would have been a reasonable expectation of success given the knowledge that Maddon et al. successfully conjugated carbohydrates to immunogenic carriers and given the fact that Maddon et al. discloses several studies where carbohydrates were conjugated to immunogenic proteins

resulting in increased immunogenicity of the carbohydrate (see pages 2-4 of Maddon et al.).

Claim 11 recites that the composition is for "reducing the effects of Human Immunodeficiency Virus (HIV) infection." The claim is drawn to a pharmaceutical composition, which is taught by the combination of references as described above. Further, as the composition in the art is the same as the claimed composition, one of ordinary skill in the art would expect the composition taught by the combination of references to also reduce the effects of HIV infection.

As for claim 12, which requires the addition of an antiviral agent, Kuo et al. does not specifically contemplate a composition comprising both the high-mannose structure and an antiviral agent.

However, it would have been obvious to one of skill in the art to combine the high-mannose structure and an antiviral agent. One of skill in the art would have been motivated to make the claimed compositions as both the high-mannose structure and an antiviral agent are useful in treating HIV (e.g., inhibiting infection via antibodies produced against the high-mannose structure or inhibiting infection via antiviral agents). One of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed compositions for the intended use of inhibiting or treating HIV infection.

Further, the courts have said: "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose . . . . [T]he

idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted) (Claims to a process of preparing a spray-dried detergent by mixing together two conventional spray-dried detergents were held to be prima facie obvious.).

Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 9 and 14 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nicole Kinsey White, PhD whose telephone number is (571) 272-9943. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nicole Kinsey White, PhD
Examiner
Art Unit 1648

/nkw/

/Stacy B. Chen/ 1-31-2008
Primary Examiner, TC1600